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THE POTENTIAL OF BANDOTAN LEAVES (*Ageratum conyzoides* L.) AS AN IMMUNOSTIMULANT AND ANTIBACTERIAL AGENT IN AQUACULTURE: A REVIEW

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ABSTRACT

Aquaculture intensification increases fish susceptibility to infectious diseases, prompting the search for natural alternatives to reduce dependence on synthetic chemicals. Bandotan leaves (*Ageratum conyzoides* L.) of the Asteraceae family contain secondary metabolites, including flavonoids, alkaloids, terpenoids, and saponins, with antibacterial, antioxidant, and immunomodulatory activities. This literature review aims to analyze the potential of bandotan leaves as a natural immunostimulant and antibacterial agent in aquaculture, focusing on their phytochemical content, mechanism of action, and safety. This study used a literature review method, conducting searches across national and international journal databases, university repositories, and research institute publications. The inclusion criteria included articles discussing the biological aspects, phytochemical content, antibacterial activity, immunomodulatory effects, physiological parameters, histology, and safety of bandotan leaves in the context of aquaculture. The results of the study showed that bandotan leaf extract effectively inhibited the growth of pathogenic bacteria in fish by disrupting cell membrane integrity and inhibiting bacterial enzymes. Its bioactive compounds enhance immune response, antioxidant activity, and reduce metabolic stress in fish. However, its application faces challenges in determining the optimal dosage, assessing histopathological effects, and managing potential respiratory distress at high concentrations. Further research is needed to optimize the formulation, understand the molecular mechanisms, and ensure the long-term safety of bandotan leaf use in sustainable fish farming systems.

Keywords: Immunostimulant, Aquaculture, Secondary Metabolites, Fish Health

1. INTRODUCTION

Bandotan leaves (*Ageratum conyzoides*) are a wild plant from the Asteraceae family that has been widely known in traditional medicine and non-conventional applications, including aquaculture. These leaves are commonly found in agricultural and plantation areas, thriving in disturbed and degraded locations[1]. In recent decades, the use of natural materials to support aquaculture has gained popularity as an alternative to synthetic chemicals, particularly in anesthesia, growth promotion, and fish immunity[2,3].

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The potential of *A. conyzoides* in aquaculture is supported by its secondary metabolites, including flavonoids, phenols, and saponins, which possess antioxidant, antibacterial, and anti-inflammatory properties. These properties make bandotan leaves a promising natural alternative for improving fish health and managing diseases in aquaculture environments[4,5]. The administration of herbal immunostimulants to fish is crucial for supporting health and productivity in aquaculture[6-7], as fish are often exposed to pathogens, such as parasites, bacteria, fungi, and viruses, which cause infections and reduce the quality of aquaculture products.

The use of herbal plants in aquaculture is not new, but their use as immunostimulants still requires further research to determine their effectiveness and mechanism of action. In addition, understanding how the active compounds in *A. conyzoides* work at the molecular level is crucial to ensuring their effectiveness as immunostimulants. Therefore, information on this is needed to determine the extent to which bandotan leaves can enhance fish growth and immune response, as well as their potential side effects and interactions with environmental factors in aquaculture.

By reducing the use of synthetic chemicals, such as antibiotics and pesticides, which can pollute the environment and negatively impact aquatic biodiversity[6-8]. In the long term, the use of *A. conyzoides* as an immunostimulant for fish can help create a sustainable aquaculture system, increase the resistance of fishery products to disease, and reduce the risk of spreading pathogens that can harm the fishing industry as a whole.

In the context of the fisheries industry's increasing focus on sustainability and cost efficiency, *A. conyzoides* offers an attractive alternative, as it is easily obtainable, relatively inexpensive, and, when used correctly, can support fish health and survival. However, comprehensive information on their mechanism of action and practical applications remains limited. This article examines the potential of bandotan leaves as a natural immunostimulant and antibacterial agent in aquaculture, based on their phytochemical content, biological activities, mechanisms of action, and applications in fish farming.

2. RESEARCH METHOD

This literature study used a literature review approach. The first step was to identify and collect scientific articles discussing *A. conyzoides* in the context of aquaculture. The literature search was conducted across national and international journal databases, university repositories, and publications from relevant research institutions. The inclusion criteria included studies discussing biological and ecological aspects, the benefits of bandotan leaves on survival rates, physiological parameters, histology, and the limitations of bandotan leaves in aquaculture.

3. RESULT AND DISCUSSION

Content of Secondary Metabolites and Nutrients

Ageratum conyzoides L., commonly known as bandotan, babadotan, or wedusan, is an erect herbaceous annual plant that usually grows to a height of 30-80 cm[9]. This plant is considered a dangerous weed, known for its ability to invade agricultural land, open land, and degraded areas, resulting in reduced crop yields and biodiversity loss. It is found in various regions of Asia, Africa, North America, the Caribbean, South America, and Oceania[10].

Ageratum conyzoides has been used in traditional medicine to treat various ailments, including burns, wounds, infections, and skin diseases. This plant contains various chemical compounds, including alkaloids, flavonoids, chromenes, benzofurans, and terpenoids, which contribute to its pharmacological activity[11]. These chemical compounds exhibit antibacterial, anti-inflammatory, analgesic, and wound-healing properties, making them valuable in pharmaceutical and agricultural applications[12].

The nutritional content of bandotan leaves has been extensively studied for its applications in various fields, including traditional medicine and animal feed. Although better known as a medicinal plant, bandotan leaves also contain several nutritional components that can support the health of organisms, including fish. The following are some secondary metabolites and nutritional content found in bandotan leaves (Table 1 and 2):

Table 1. Secondary metabolite compounds in *A. conyzoides*

Secondary metabolites	Reference
Tannins, flavonoids, coumarins, free quinones, anthraquinones, alkaloids, sterol-triterpenes, terpenoids, saponins, anthocyanins, volatile oils	[13]
Tannins, alkaloids, flavonoids, phenols, glycosides, cardiac glycosides, reducing sugars, and saponins	[14]
alkaloids, tannins, phenols, saponins, coumarins, essential oils, and flavonoids	[15]
saponins, tannins, terpenoids, alkaloids, phenols, and flavonoids	[16]
Coumarin, Methyl Tetracosanoate, 3°Butyl Triacosanoate, 23-Pentatetraacontanone, and 3,4-seco-lup-20 (29)-en-3-one	[17]

Table 2. Nutritional content of *A. conyzoides*

Nutrients	Reference
Vitamins, including ascorbic acid (33.36 mg/100g), thiamine (0.22 mg/100g), riboflavin (0.16 mg/100g), niacin (0.07 mg/100g), and tocopherol (0.61 mg/100g); Minerals including zinc (5.75 mg/100g), iron (2.52 mg/100g), calcium (0.51 mg/100g), phosphorus (0.23 mg/100g), and magnesium (0.11 mg/100g)	[18]
crude protein (24.53%), crude lipid (3.78%), crude fiber (18.89%), and carbohydrates (36.81%); sodium (88.50 mg/100g), potassium (139.10 mg/100g), calcium (220.60 mg/100g), magnesium (110.13 mg/100g), iron (22.73 mg/100g), zinc (43.50 mg/100g), and phosphorus (380.13 mg/100g)	[19]
carbohydrates (84.97%), crude protein (1.53%), crude fat (3.27%), and moisture (9.00%)	[16]

Ageratum conyzoides leaves contain various secondary metabolites, including alkaloids, flavonoids, coumarins, essential oils, tannins, and terpenoids, which exhibit biological activity and therapeutic properties. These compounds have been studied for their potential to treat various diseases and for their role in plant protection and growth inhibition. According to Bamba et al.[13], alkaloids and flavonoids have antimicrobial and anti-inflammatory properties. Chawla et al.[17] stated that coumarins and tannins contribute to the therapeutic use of plants, including the treatment of skin diseases and antioxidant activity.

Terpenoids and sterols are involved in the insecticidal and antimicrobial activities of plants, making them useful in medicine and agriculture. At the same time, the presence of phenolics and flavonoids is associated with plants' ability to inhibit bacterial growth and scavenge free radical[14]. These plants also contain non-essential and potentially harmful elements, such as lead and cadmium, which may limit their use as a food source but highlight their suitability for medicinal and agricultural applications [20].

Ageratum conyzoides Leaves are an Antibacterial Agent.

Ageratum conyzoides has various health benefits for humans, animals, and fish. One of the main benefits of this plant is its antibacterial properties, which can help improve fish health, especially in combating

bacterial infections common in aquaculture environments. The antibacterial ability of bandotan leaves has been extensively studied in recent years, given the importance of maintaining fish health in aquaculture.

Ageratum conyzoides has been shown to have significant antibacterial activity against various bacterial strains, including *Staphylococcus aureus, Escherichia coli,* and *Salmonella enteritidis*[21,22]. According to Daula et al.[23], methanolic extracts of the plant, as well as fractions soluble in n-hexane, chloroform, and ethyl acetate, have shown varying levels of antibacterial activity, with inhibition zones ranging from 9.50 mm to 19.40 mm. Furthermore, Namuga et al.[24] stated that the use of *A. conyzoides* as a natural antibacterial agent in aquaculture can help reduce the spread of bacterial infections in fish.

Flavonoids in *A. conyzoides* are known to bind to bacterial cell membranes, thereby disrupting bacterial structural integrity[25]. In addition, the terpenoids in this plant inhibit the enzymes bacteria need for growth[26]. This mechanism is crucial because pathogenic bacteria in aquaculture environments can multiply rapidly, leading to infections that reduce the quality and quantity of fish production.

Bandotan Leaves in Enhancing Fish Immunity

The use of *A. conyzoides* in aquaculture has primarily been explored for its sedative and antimetabolic properties rather than for directly enhancing fish immunity. While *A. conyzoides* leaves contain essential oils and saponins with various applications in fisheries, their role in enhancing fish immunity is not explicitly documented in the provided research papers. However, the potential of *A. conyzoides* leaves in aquaculture can be assessed from their effects on fish metabolism and stress reduction, which indirectly support fish health and immunity.

According to Sulmartiwi et al.[27], *A. conyzoides* leaves have a sedative effect on koi (*Cyprinus carpio*), where essential oils from the leaves are used to reduce fish metabolism during transport. This reduction in metabolic rate helps minimize stress, a crucial factor for maintaining fish health during transportation. The antimetabolic properties of *A. conyzoides* leaves were also evaluated in common carp fry, showing significant effects on post-transportation digestion and respiration. This indicates that *A. conyzoides* can help manage metabolic changes caused by stress. Additionally, Aini et al.[28] found that the sedative properties of *A. conyzoides* are highly beneficial during fish transportation, as stress can elevate metabolism and increase mortality. The use of this plant extract can help reduce metabolic rates and improve post-transport survival rates.

According to Ambwani et al.[29], *A. conyzoides* exhibits vigorous antioxidant activity, which is important for protecting fish against oxidative stress. The plant extract has demonstrated significant radical-scavenging activity, which can help maintain cell health and boost the immune system. This is demonstrated by increased lymphocyte proliferation, particularly affecting B and T cells. This indicates that the plant can stimulate the immune system, making fish more resistant to infection and disease.

In addition to its stress-reducing and immunomodulatory effects, *A. conyzoides* has been evaluated as a dietary supplement. When used as a partial replacement for corn in the diet of African catfish (*Clarias gariepinus*), it supported growth performance and improved hematological and serological profiles, indicating a positive impact on fish health[30]. Compounds such as saponins, while bioactive, can cause irritation or adverse reactions in gill tissues when used improperly[31]. Flavonoids isolated from *A. conyzoides* leaves have been shown to have antioxidant activity. The ethanol extract of these leaves showed moderate antioxidant activity with an LC_{50} value of 118.19 µg/mL, indicating their potential to neutralize free radicals rather than increase their formation[32].

Safety and Toxicology

The compounds in *A. conyzoides* leaves have the potential to affect fish's respiratory systems. Several studies have shown that flavonoids and alkaloids can reduce oxygen levels in fish, leading to respiratory disorders. Disruption of the fish's respiratory process can cause stress, weakness, and even death, especially at high concentrations of leaf extract. When fish are exposed to water contaminated with toxic compounds, gas exchange between blood and water is disrupted, thereby affecting the oxygenation of their tissues[33]. Fish exposed to hypoxic conditions or toxic compounds often exhibit increased respiratory rates and altered behavior as compensatory mechanisms to maintain oxygen uptake. This response can be exacerbated by the presence of flavonoids and alkaloids, which can further stress the fish and impair their ability to cope with low oxygen levels[34].

The application of bandotan leaves at a dose of 1 g/L has been shown to increase the survival rate of juvenile catfish during closed-system transport. This indicates the potential benefits of using bandotan leaves to improve fish resilience under stressful conditions. Although survival increased, histological analysis revealed abnormalities in the gills, including fusion, haemorrhage, and telangiectasia. These changes indicate that while bandotan leaves may offer some protective benefits, they can also cause structural damage to the gills. This is a serious concern because the gills are vital organs for respiration and osmoregulation[35].

Challenges in Aquaculture Application

The application of *A. conyzoides* in aquaculture poses several challenges, despite its potential as a natural anaesthetic and antimicrobial agent. These challenges primarily revolve around optimizing its use, understanding its effects on fish physiology, and ensuring environmental safety. Some challenges and considerations to address include determining dosage, assessing physiological effects, and integrating with other strategies.

Firdaus et al.[36]; Syamsiyah et al.[37] reported that bandotan leaves affect blood glucose levels and survival rates during fish transport. Although they can reduce stress-induced glucose spikes, their impact on long-term health and survival during maintenance remains unclear and warrants further investigation. Histological studies of fish gills have revealed potential abnormalities, such as fusion and hemorrhage, when bandotan leaves are used, highlighting the need for careful monitoring of physiological effects[35]. Integrating bandotan leaves with other disease management strategies, such as essential oils or other natural extracts, may enhance their effectiveness. However, understanding the interactions and potential synergistic effects among different natural compounds remains a challenge[38].

4. CONCLUSION

Ageratum conyzoides leaves show significant potential as natural immunostimulants and antibacterial agents in aquaculture, owing to their high levels of secondary metabolites, particularly flavonoids, alkaloids, terpenoids, and saponins. Its antibacterial activity is effective against various aquatic pathogens through mechanisms of cell membrane disruption and inhibition of vital bacterial enzymes. Its immunomodulatory properties enhance lymphocyte proliferation and antioxidant activity, while its sedative effects help reduce metabolic stress during fish transportation. Nevertheless, its application requires caution due to the potential for histopathological effects on gills and respiratory distress at high doses. Key challenges include standardizing optimal dosages, gaining a deeper understanding of molecular mechanisms, and evaluating long-term safety.

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